Original Article

Frequency of Pseudomembranous Colitis in Antibiotic Associated Diarrhea

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Objectives: The objective of this study is to determine the frequency of Pseudomembranous colitis in antibiotic associated diarrhoea in tertiary care hospital.

Methods: Two hundred and fifty patients, who fulfilled the inclusion criteria, were enrolled in the study. The antibiotic being taken by the patients was documented. No specific therapy or diet for the prevention of diarrhea was prescribed, except for the withdrawal of antibiotic and introduction of antiperistaltic agent. After 3 days of starting diarrhea, stool culture for Clostridium difficile infection was done and if it was found to be positive then patients were subjected to sigmoidoscopy/colonoscopy to confirm the presence of pseudomembranous colitis.

Results: Out of two hundred and fifty patients,159 patients (63.6%) were, 12-40 years old, 59 patients (19.6%) were between 41-60 years of age while 42 patients (16.8%) were between 61-70 years of age. 130 patients (52.0%) were male and remaining 120 patients (48.0%) were female. Stool culture for Clostridium was positive in 63 patients (25.2% of total) and negative in 187 patients (74.8% of total). Pseudomembranous colitis was noted in 31 patients (12.4%) on lower GI endoscopy.

Conclusions: Considerable number of antibiotic associated diarrhea cases were found to have evidence of Pseudomembranous colitis.

Keywords: Pseudomembranous colitis, diarrhea and antibiotic associated diarrhea.

Introduction

Antibiotic-associated diarrhea (AAD) is defined as the diarrhea that occurs in association with the administration of antibiotics after excluding other causes of diarrhea. It can be a significant problem for patients needing antibiotic therapy. It can affect patient compliance resulting in incomplete duration of therapy and development of microbial resistance[1]. Frequency of Antibiotic-associated diarrhoea varies from 5-39 % depending on the antibiotic type.[2]

Clostridium Difficile infection is responsible for approximately 20% cases of Antibiotic-associated diarrhea.[3,4] Pseudomembranous colitis (PMC) is characterized by inflammation of colonic wall with inflammatory debris and cells and distinctive patches of yellowish gray exudates, ulcerations or ovoid plaques, separated by normal or hyperemic mucosa. PMC complicates about 50 % cases of *Clostridium Difficile* infection and about 10 % cases of Antibiotic-associated diarrhea.[3,4]

Klebsiella pneumonia, Staphylococcus *aureus*, *Candida* albicans, and candida tropicalis might also contribute to the development of Antibiotic-associated diarrhea.[5] Up to 5% of healthy adults and majority of infants and children are asymptomatic carriers of *Clostridium Difficile*.[3,6]

Clostridium difficile is a Gram-positive spore bearing anaerobic bacteria and is commonly present in the stools of 5 % of healthy adults and in about 15-70 % of infants.[3-5] The majority of hospitalized patients infected by *C. difficile* are asymptomatic carriers who serve as silent reservoirs in hospital environment.[6] However *C. difficile*-associated disease (CDAD) is a serious condition with mortality up to 25 % in frail elderly people[7] and is now recognized as the primary cause of hospital acquired colitis in patients who receive antibiotics, chemotherapeutics or other drugs that alter their normal flora. *C. difficile* infection was initially considered as a consequence of antibiotic intake and not as a life threatening disease. During the recent outbreaks of CDAD in the West, a higher number of cases involving toxic megacolon, colectomy or death have been reported.[8] The mutant hypervirulent strain was typed as NAP1/BI/027 (North American PFGE type I/restriction endonuclease analysis BI/ribotype 027).[9] It was found to produce greater than 16 times toxin A and 23 times toxin B in addition to the binary toxin.[10]

C. difficile is also being reported more frequently even from non hospital-based settings, such as from the community.[14] Domestic as well as wild animals are probably transmitting this as the same ribotypes found in them were found to be associated with human infection.

Material And Methods

It was a cross sectional study, done in emergency department, OPD and Indoor Department of Medical Unit-III of Services Hospital Lahore. Sampling was done by purposive non-probability technique. Study was conducted for six months. Two hundred and fifty patients of antibiotic associated diarrhea were enrolled in this study. Patients who took even a single dose of antibiotic and developed diarrhea at least 3 days afterwards and no history of diarrhea in preceding 2 weeks before starting antibiotics was included in this study. Patients having other causes of chronic diarrhea like IBS, inflammatory bowel diseases, Celiac disease, colorectal carcinoma, thyrotoxicosis and diabetes mellitus, which were diagnosed on the basis of previous history and laboratory test and use of laxatives were excluded. The antibiotic being taken by the patients was documented. No specific therapy or diet for the prevention of diarrhea was prescribed, except for the withdrawal of antibiotic and introduction of antiperistaltic agent. After 3 days of starting diarrhea, stool culture for Clostridium difficile infection was done, if it was found to be positive then patient were subjected to sigmoidoscopy/colonoscopy to confirm the presence of Pseudomembranous colitis. The data was entered and analyzed by SPSS version 10.0.

Results

Out of 250 patients, 159 patients (63.6%) were 12-40 years old, 59 patients (19.6%) were 41-60 years of age while 42 patients (16.8%) were between 61-70 years of age. Mean age of patients was 36.94 (±16.239) 130 patients (52.0%) were male and remaining 120 patients (48.0%) were female. In this study most offending drug for PMC causation was found to be Clindamycin (19.3% of patients taking

**Table-1:** Frequency of Pseudomembranous colitis and sex distribution.

Number (n=250)		%
Age (Years)		
12-40	159	63.6
41-60	49	19.6
61-70	42	16.8
Sex Distribution		
Male	130	52.0
Female	120	48.0

the drug developed this condition). Erythromycin and Ceftriaxone were among the second and third culprit agents respectively. Stool culture for Clostridium was positive in 63 patients (25.2% of total) and negative in 187 patients (74.8% of total). Pseudomembranous colitis was noted in 31 patients (12.4%) lower GI endoscopy.

Table-2: Distribution of pseudomembranous colitis with respect to the use of different Antibiotics.

Antibiotic Name	No. of patients who used the antibiotic	No. of patients who d-loped pseudome-mbranous colitis (n)
Clindamyoine	52	10 (19.33%)
Erythromyoine	28	04 (14.28%)
Co-amoucicilin	62	04 (6.45%)
Ciprofloxcacin	44	05 (11.36%)
Ceftriazone	24	03 (12.5%)
Clarithromicin	28	03 (10.71%)
Amoxicillin	12	01 (8.33%)

Fig-1: Stool Culture results in Patients with Antibiotic Associated Diarrhea.
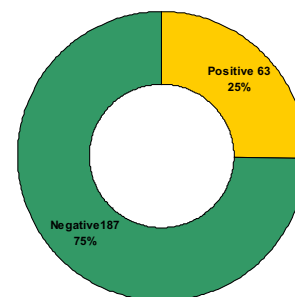
Discussion

The diagnosis of Pseudomembranous colitis in this study was based upon the presence of positive sigmoidoscopic/colonoscopic findings in patients with antibiotic associated diarrhea with positive stool culture for clostridium. Using this criterion, out of two fifty patients, 31 were found to have Pseudomembranous colitis. In our region, there are limited studies on *C. difficile*-Associated Diarrhea, (CDAD) probably due to the lack of technology and the difficulty in culturing the pathogen.

This is the first study in Pakistan that reports the frequency of Pseudomembranous colitis and CDAD among patients with antibiotic associated diarrhea. Available reports from India estimate the prevalence

of CDAD of about 15-30 % in patients taking antibiotics[15-19]. Gupta & Jadav[20] reported 25.3 per cent isolation of *C.difficile* from diarrheal patients of all age groups. Vaishnavi *et al*[7] reported 30 per cent positivity for *C. difficile* toxin in hospitalized patients. When only adult population was investigated, the positivity for *C. difficile* toxin was 19.4 per cent in the antibiotic receiving hospitalized patients[21]. Some studies from United States reveal the frequency of Clostridium difficile infection of about 20-25% and of Pseudomembranous colitis of about 10% in patients of antibiotic associated diarrhea.[3,4] These findings are comparable with our results where frequency of CDAD among patients with AAD was noted 25.2% and of PMC about 12.4%. Kang *et al*[22] reported that *C. difficile*-associated diarrhoea was more common in the post transplantation period in India than in developed countries. Vaishnavi *et al*[23] reported the association of *C. perfringens* with antibiotic associated diarrhoea either by itself or in synergy with *C. difficile* infection. Balamurugan *et al*[24] reported overgrowth of *C. difficile* in the stool of Indian patients with ulcerative colitis compared to healthy controls using real time PCR. Due to difference in demographic profile, injudicious use of antibiotics in our community, depressed nutritional and immunological status, and global emergence of resistant strain (BI/NAP1/027), our population has more propensity of acquiring CDAD. In addition to this due to poor sanitary condition and insufficient supply of clean drinking water, feco-oral transmission of infections is common. Prevention of *C. difficile* infection is challenging. A change in antibiotic policy and implementation of standard infection control measures reduces the incidence of *C. difficile* symptomatic infections. Combined approach, involving effective control measures, the use of rapid and sensitive techniques for laboratory diagnosis as well as prudent use of antibiotics, is necessary to reduce morbidity and mortality due to *C. difficile* associated infections in hospitalized patients. It certainly highlights the importance of public awareness regarding the judicious use of antibiotics. We urge the clinicians that while advising antibiotics, they must have a high index of clinical suspicion of PMC, if the patients subsequently develop diarrhea after taking therapy. Furthermore, screening tests can be incorporated for general population, if this clinical problem would found to be significantly high in future large scale, probability studies. This may reduce morbidity and mortality associated with this grave but treatable condition.

There are a few limitations to the study results. Firstly, this study was conducted on small scale. Sampling of the patients was done by non-probability purposive method. Therefore the results obtained cannot be generalized. We only analyzed the association of PMC with different antibiotics but preference or percentage of patients receiving a particular antibiotic many influence this results, as there may be over prescription of certain antibiotics. To overcome the above mentioned problems following suggestions should be taken into consideration:

1. A large scale, population based study is needed to achieve results, which can be applied to general population.
2. Sampling should be done by probability techniques. Many of the patients who had been diagnosed as cases of antibiotic associated diarrhea and pseudo-membranous colitis did not have knowledge of their problem and subsequent complications. So it is suggested that screening for pseudomem-branous colitis should be done meticulously.

Conclusion

Based on the results obtained from our study, it is concluded that considerable number of antibiotic associated diarrhea cases were found to have evidence of Pseudomembranous colitis. Early detection of Pseudomembranous colitis is of vital importance, as with appropriate care we can reduce morbidity and mortality. The results of this study support our objectives. A large scale population based study is required for achieving significant results, which can be generalized. Following features can be highlighted from study:

1. *C. difficile* associated disease is a growing nosoc-omial and public health problem.
2. Pseudomembranous colitis is an important comp-lication of antibiotic associated diarrhea.
3. Most culprit drug was found to be Clindamycine followed by Erythromycine and Ceftriaxone respectively.
4. Clinical suspicion is more important because stool assays for diagnosing CDAD are not widely ava-ilable. Hospitalized patients receiving antibiotics for their ailments are at greater risk of acquiring.
5. Infection control procedures that should be foll-owed to prevent spread of the CDAD include environmental hygiene, use of phenolic disinfectant washing hands with ordinary soap and water or using 0.03 percent Triclosan and isolating patients with CDAD.

6. Preventing *C. Difficile* infection offers a potentially significant improvement in patient's outcomes, as well as a reduction in hospital, costs and resource expenditures.

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